EU-PEARL
EU PATIENT-CENTRIC
CLINICAL TRIAL PLATFORMS

Precision Medicine and Clinical Trials

ISCIII y UIMP curso: "Medicine de precisión: Ciencia y tecnología al servicio de la transformación del sistema sanitario". 30 Junio - 2 Julio de 2021

30 Junio 2021

Lucinda Cash-Gibson, PhD,
Vall d´Hebron Institute for Research (VHIR), Barcelona, Spain.

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 853966. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA, and Children's Tumour Foundation, Global Alliance for TB Drug development non-profit organisation, Springworks Therapeutics Inc.
This presentation reflects the authors' view. Neither IMI nor the European Union, EFPIA or any Associated Partners are responsible for any use that may be made of the information contained.

Drug development - Challenges

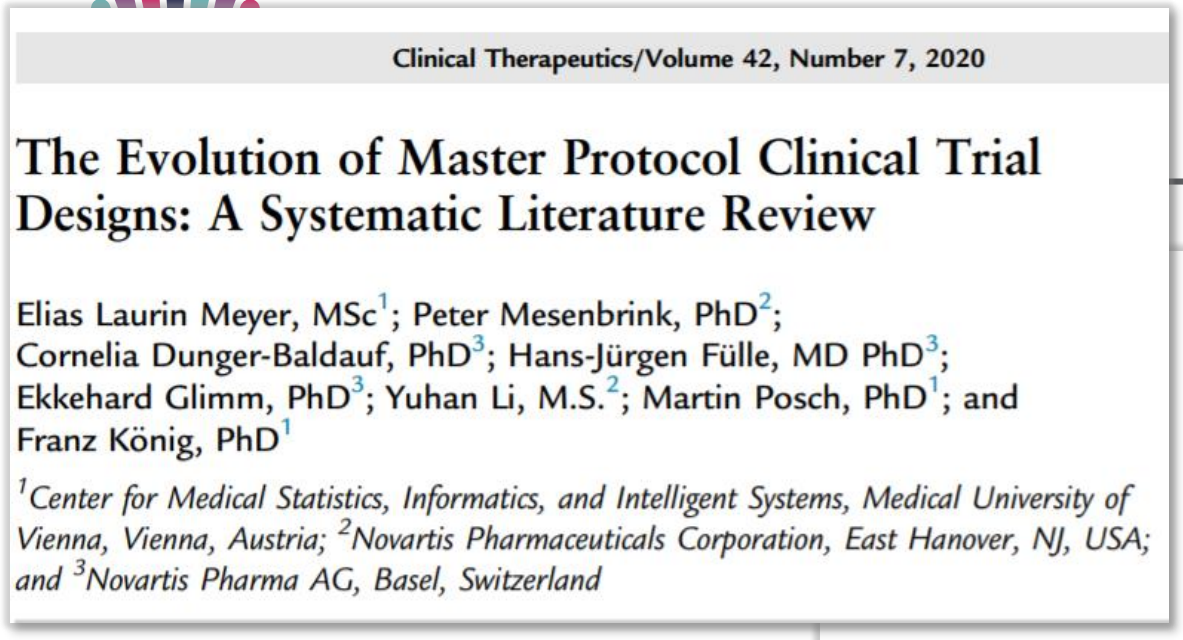
- Advancements in fundamental and applied biomedical research, yet translation into treatments has become **inefficient, expensive, slow, insufficiently tailored**.
- Investigating 1-2 interventions in single disease can be expensive and challenging to execute, and important questions remain unanswered. **High unmet clinical needs**.
- Challenge to **recruit patients** in “Precision medicine” trials aiming to evaluate targeted treatments (e.g. rare diseases).
- **Potential causes**: (i) siloed, competitive development process focused on single compounds, (ii) insufficient collaboration among stakeholders (iii) limited aligned patient-centric approach by stakeholders, (iv) limited focus on individual tailored treatments.
- Has **led to shortages**: (i) investigators & sites for phase 2-3 clinical trials, (ii) patients for enrollment, (iii) sharing knowledge and use of real-world data, (iv) investigations of combination treatments from different sponsors.

Drug development – Novel ways forward

- **Master protocol trial designs** considered to be **more efficient** than traditional *"one drug, one trial"* paradigm in certain situations/questions.

- Different types of designs (e.g., umbrella, platform, basket)
- Enable study **one or more interventions in one or more disease area, without setting up separate studies**.
- Uses common screening framwork to identify interventions for which patients may be eligible, **creating more opportunities for patients**.
- Often include periodic interim analyses to determine futility or success, and potentially **allow patients to be re-assigned** to other arms/treatments.
- Began in early 2000s, grown significantly in last few years. Majority in oncology, yet increasingly used in other areas e.g Alzheimer's disease, infectious diseases.

Growing literature...



Clinical Therapeutics/Volume 42, Number 7, 2020

The Evolution of Master Protocol Clinical Trial Designs: A Systematic Literature Review

Elias Laurin Meyer, MSc[1]; Peter Mesenbrink, PhD[2]; Cornelia Dunger-Baldauf, PhD[3]; Hans-Jürgen Fülle, MD PhD[3]; Ekkehard Glimm, PhD[3]; Yuhan Li, M.S.[2]; Martin Posch, PhD[1]; and Franz König, PhD[1]

[1]Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria; [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; and [3]Novartis Pharma AG, Basel, Switzerland

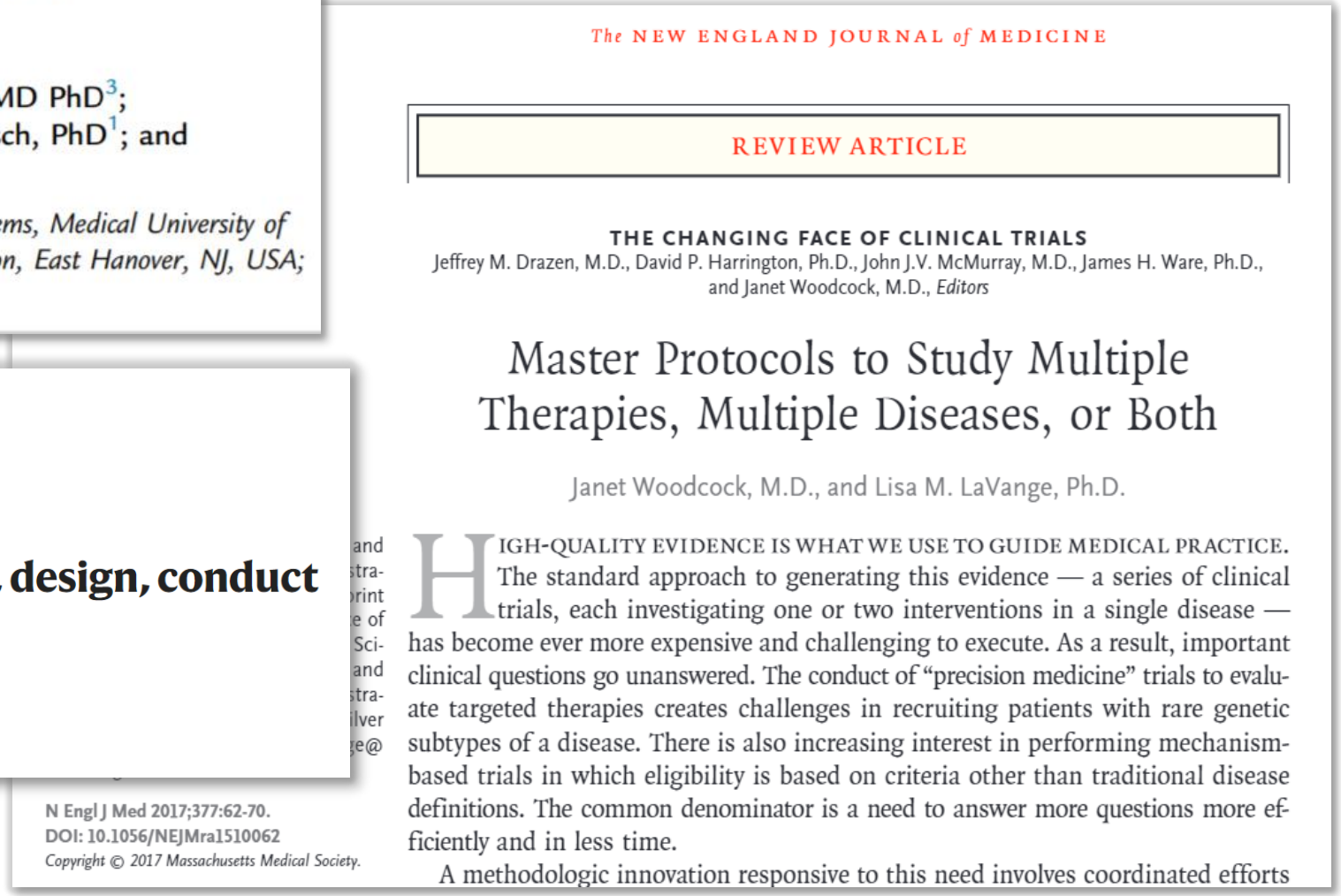
Perspective | Published: 28 August 2019

OPINION

Adaptive platform trials: definition, design, conduct and reporting considerations

The Adaptive Platform Trials Coalition

Nature Reviews Drug Discovery **18**, 797–807 (2019) | Cite this article



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both

Janet Woodcock, M.D., and Lisa M. LaVange, Ph.D.

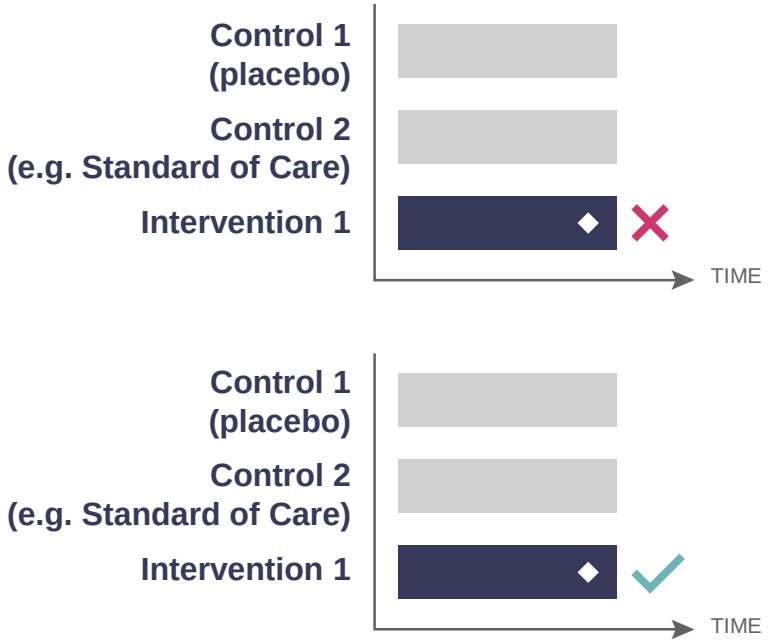
HIGH-QUALITY EVIDENCE IS WHAT WE USE TO GUIDE MEDICAL PRACTICE. The standard approach to generating this evidence — a series of clinical trials, each investigating one or two interventions in a single disease — has become ever more expensive and challenging to execute. As a result, important clinical questions go unanswered. The conduct of "precision medicine" trials to evaluate targeted therapies creates challenges in recruiting patients with rare genetic subtypes of a disease. There is also increasing interest in performing mechanism-based trials in which eligibility is based on criteria other than traditional disease definitions. The common denominator is a need to answer more questions more efficiently and in less time.

A methodologic innovation responsive to this need involves coordinated efforts

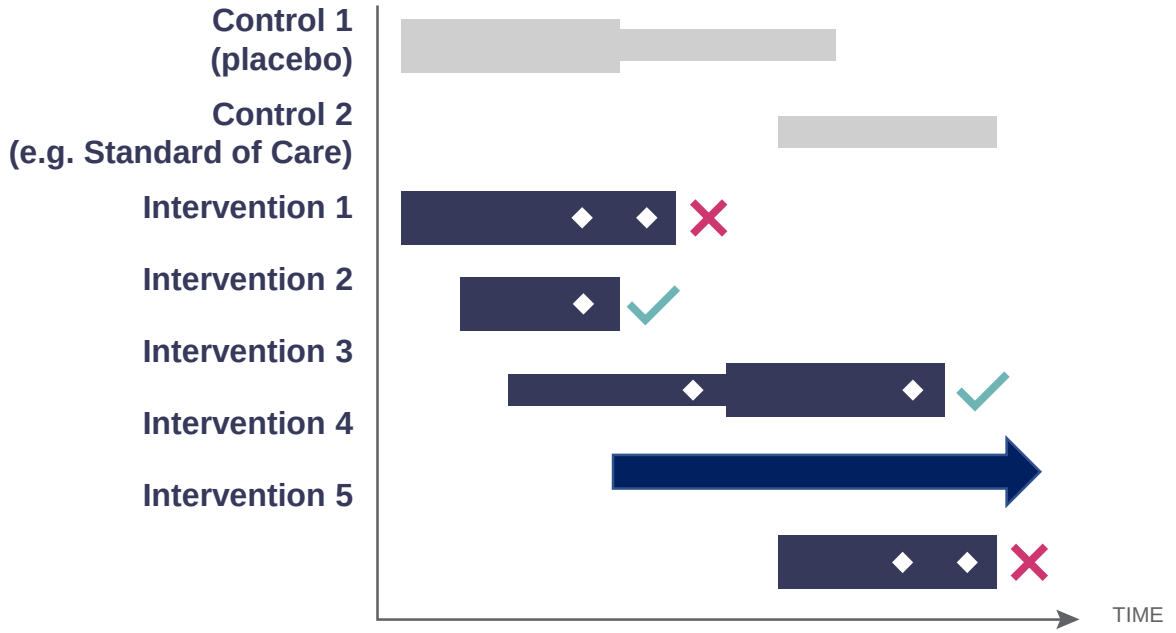
N Engl J Med 2017;377:62-70.
DOI: 10.1056/NEJMra1510062

Different trial approaches

Traditional Clinical Trial Approach



Adaptive Platform Trial Approach



(INTERIM) ANALYSIS STOP FOR FUTILITY GRADUATE TO PH 3

EU-PEARL
EU PATIENT-CENTRIC
CLINICAL TRIAL PLATFORMS

SHAPING THE FUTURE OF CLINICAL TRIALS

November 2019 – April 2023

Project Coordinator: Joan Genescà *(VHIR)*

Project Lead: Ann Van Dessel *(Janssen Pharmaceutica)*

EFPIA contribution: 14.2 MM €
IMI2 JU funding: 12 MM €

Transforming the future of drug development by creating a sustainable entity available for industry and academia to conduct platform trials in any disease area, co-designed by patients.

Strategic Public-Private Alliance

EUROPEAN UNIVERSITY HOSPITAL ALLIANCE (EUHA) HOSPITALS

Vall d'Hebron Institut de Recerca
Vall d'Hebron
Erasmus MC
Assistance Publique Hôpitaux de Paris
UniSR Università Vita-Salute San Raffaele
Medizinische Universität Wien
King's College London
KU Leuven
Charité Universitätsmedizin Berlin

OTHER HOSPITALS

LMU Klinikum der Universität München

UNIVERSITIES

University of Oxford
The University of Manchester
Università degli Studi di Milano
Newcastle University
Tartu Ülikool 1632 Universitas Tartuensis

PATIENT ORGANISATION

EPF European Patients Forum

DATA, STATISTICS

The European Institute For Innovation Through Health Data
Berry Consultants Statistical Innovation
CUSTODIX

REGULATOR

Paul-Ehrlich-Institut
eurosscan

PROJECT MANAGEMENT

teamit Research

EUROPEAN RESEARCH INFRASTRUCTURES

eatris
ECRIN European Clinical Research Infrastructure Network

BIOPHARMACEUTICAL COMPANIES / EFPIA/ ASSOCIATED PARTNERS

AstraZeneca
Novartis
Janssen
Allergan
novo nordisk
Otsuka
teva
Sanofi
Pfizer
TB Alliance Global Alliance for TB Drug Development
SpringWorks Therapeutics
Children's Tumor Foundation Ending NF Through Research
Servier

imi innovative medicines initiative
efpia
SpringWorks Therapeutics
TB Alliance
Children's Tumor Foundation Ending NF Through Research

Develop Integrated Research Platform (IRP)

Novel clinical development concept, common **enabling framework** for platform trials, centers around a **master protocol**

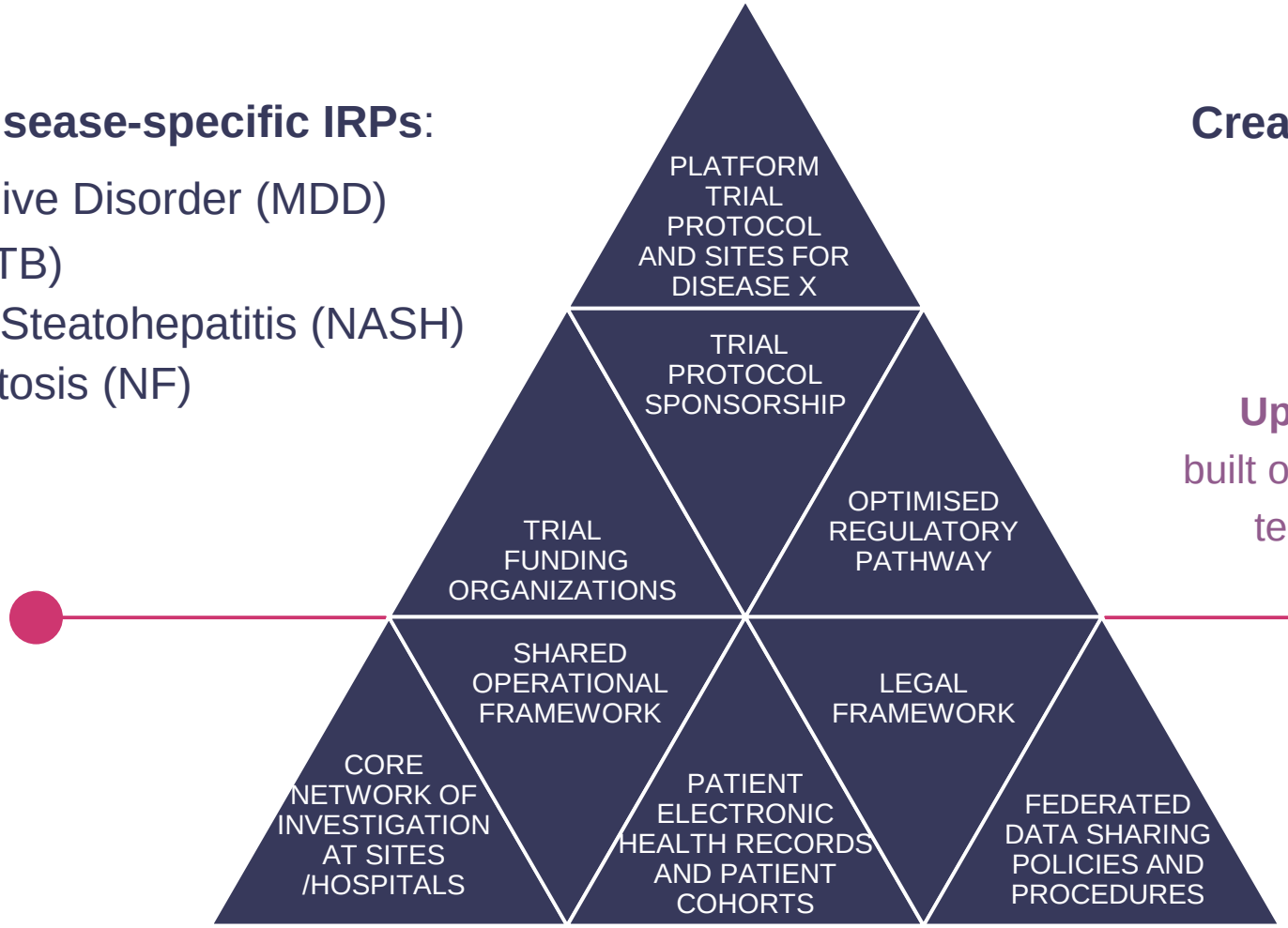
Uses **existing infrastructure of hospitals and federated patient data** in design, planning and execution to accomate multi-sourced interventions

Ensures **optimized regulatory pathway** for the novel treatments has been established

EU-PEARL IRP Concept

Create four disease-specific IRPs:

- Major Depressive Disorder (MDD)
- Tuberculosis (TB)
- Non-Alcoholic Steatohepatitis (NASH)
- NeuroFibromatosis (NF)



Create a disease-agnostic IRP

Upper disease specific part - built on platform trial design which will test multi-sourced treatments

Underlying, enabling, disease-agnostic part

What will EU-PEARL deliver?

1 A trusted **sustainable entity** ready to setup and coordinate the operation of IRP **in any disease**.

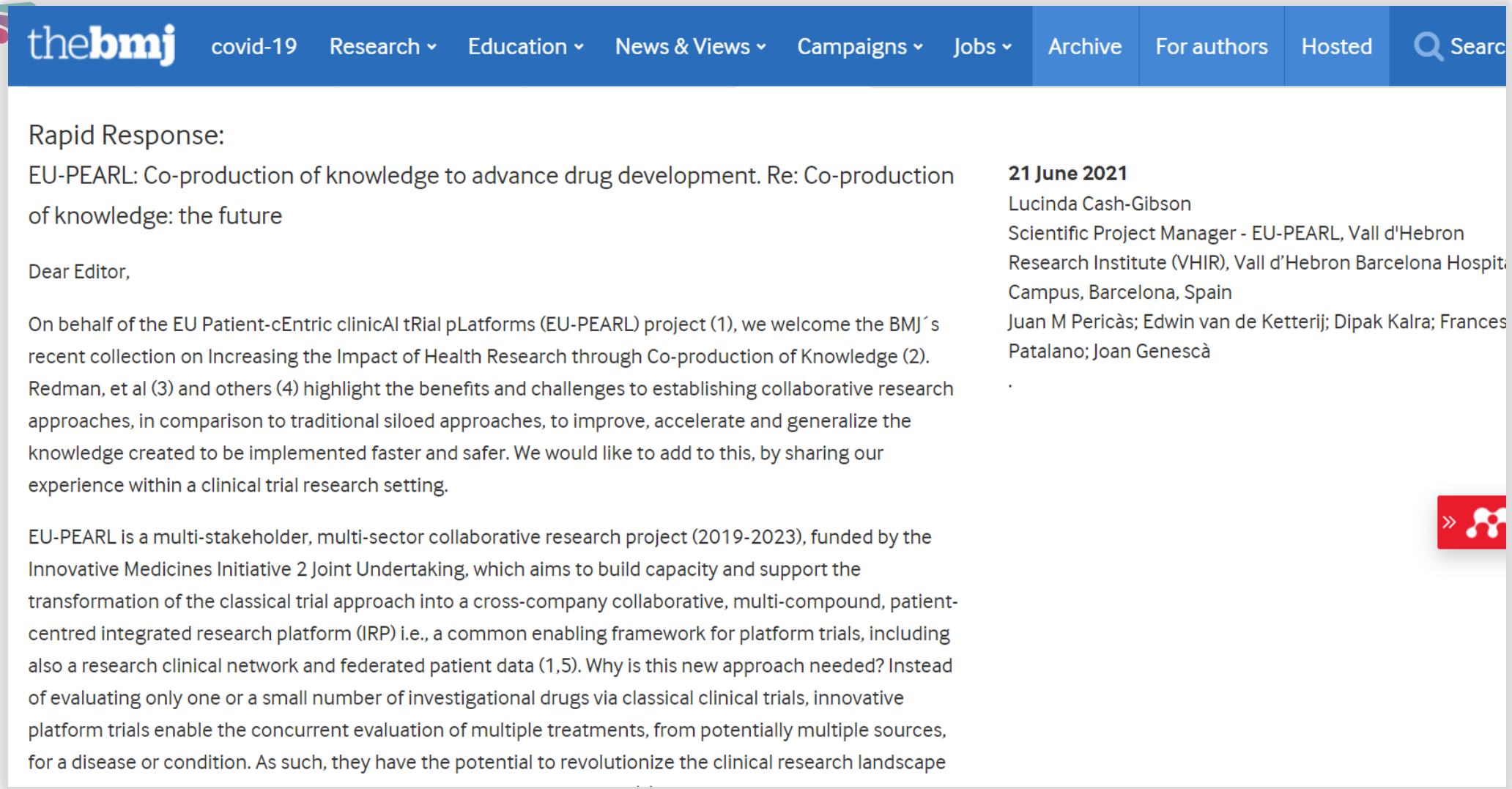
2 **Clinical Trial Platform Framework** that can be used **for any disease (Disease-agnostic IRP)**, and **four specifics**

3 **Four** disease trial-ready **clinical networks**

- Major Depressive Disorder (MDD)
- Tuberculosis (TB)
- Non-Alcoholic Steatohepatitis (NASH)
- Neurofibromatosis (NF)

4 **Patient Engagement Platform** and **materials**

Co-producing Knowledge and Building Capacity...



thebmj covid-19 Research Education News & Views Campaigns Jobs Archive For authors Hosted Searc

Rapid Response:

EU-PEARL: Co-production of knowledge to advance drug development. Re: Co-production of knowledge: the future

Dear Editor,

On behalf of the EU Patient-cEntric clinicAl tRial pLatforms (EU-PEARL) project (1), we welcome the BMJ´s recent collection on Increasing the Impact of Health Research through Co-production of Knowledge (2). Redman, et al (3) and others (4) highlight the benefits and challenges to establishing collaborative research approaches, in comparison to traditional siloed approaches, to improve, accelerate and generalize the knowledge created to be implemented faster and safer. We would like to add to this, by sharing our experience within a clinical trial research setting.

EU-PEARL is a multi-stakeholder, multi-sector collaborative research project (2019-2023), funded by the Innovative Medicines Initiative 2 Joint Undertaking, which aims to build capacity and support the transformation of the classical trial approach into a cross-company collaborative, multi-compound, patient-centred integrated research platform (IRP) i.e., a common enabling framework for platform trials, including also a research clinical network and federated patient data (1,5). Why is this new approach needed? Instead of evaluating only one or a small number of investigational drugs via classical clinical trials, innovative platform trials enable the concurrent evaluation of multiple treatments, from potentially multiple sources, for a disease or condition. As such, they have the potential to revolutionize the clinical research landscape

21 June 2021

Lucinda Cash-Gibson
Scientific Project Manager - EU-PEARL, Vall d'Hebron Research Institute (VHIR), Vall d'Hebron Barcelona Hospit Campus, Barcelona, Spain
Juan M Pericàs; Edwin van de Ketterij; Dipak Kalra; Frances Patalano; Joan Genescà
.

EU-PEARL
EU PATIENT-CENTRIC
CLINICAL TRIAL PLATFORMS

STAY connected!

VISIT OUR WEBSITE

www.eu-pearl.eu

WRITE TO US

For general enquiries

info@eu-pearl.eu

For media enquiries

press@eu-pearl.eu

FOLLOW US

SUBSCRIBE TO OUR NEWSLETTER

Sign up to stay informed

Subscribe here to our newsletter and stay updated on the latest developments:

Full Name*

Email*

SUBSCRIBE TO NEWSLETTER

imi innovative medicines initiative efpia SpringWorks THERAPEUTICS TB Alliance CHILDREN'S TUMOR FOUNDATION

THANK YOU
FOR YOUR ATTENTION

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 853966. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA, and Children's Tumour Foundation, Global Alliance for TB Drug development non-profit organisation, Springworks Therapeutics Inc.
This presentation reflects the authors' view. Neither IMI nor the European Union, EFPIA or any Associated Partners are responsible for any use that may be made of the information contained.

COVID-19 trials

Clinical Trials in Global Health 4

How COVID-19 has fundamentally changed clinical research in global health

Jay J H Park, Robin Mogg, Gerald E Smith, Etheldreda Nakimuli-Mpungu, Fyezah Jehan, Craig R Rayner, Jeanine Condo, Eric H Decloedt, Jean B Nachega, Gilmar Reis, Edward J Mills

COVID-19 has had negative repercussions on the entire global population. Despite there being a common goal that should have unified resources and efforts, there have been an overwhelmingly large number of clinical trials that have been registered that are of questionable methodological quality. As the final paper of this Series, we discuss how the medical research community has responded to COVID-19. We recognise the incredible pressure that this pandemic has put on researchers, regulators, and policy makers, all of whom were doing their best to move quickly but safely in a time of tremendous uncertainty. However, the research community's response to the COVID-19 pandemic has prominently highlighted many fundamental issues that exist in clinical trial research under the current system and its incentive structures. The COVID-19 pandemic has not only re-emphasised the importance of well designed randomised clinical trials but also highlighted the need for large-scale clinical trials structured according to a master protocol in a coordinated and collaborative manner. There is also a need for structures and incentives to enable faster data sharing of anonymised datasets, and a need to provide similar opportunities to those in high-income countries for clinical trial research in low-resource regions where clinical trial research receives considerably less research funding.

Lancet Glob Health 2021; 9: e711–20

See Comment page e575

This is the fourth in a Series of four papers about clinical trials global health

***Panel 2:* WHO's Solidarity I trial**

The Solidarity I trial (ISRCTN83971151) is a multinational randomised clinical trial, co-sponsored by WHO and participating countries.[69] The Solidarity I trial enrols hospitalised adults (aged ≥18 years) with confirmed COVID-19 to compare four treatment options against standard of care to assess their relative effectiveness against COVID-19. Study drugs include remdesivir, hydroxychloroquine, lopinavir (fixed-dose

***Panel 4:* RECOVERY trial**

The Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial (ISRCTN50189673; NCT04381936) is a large adaptive platform trial with a factorial design that is evaluating multiple different interventions for hospitalised patients with SARS-CoV-2 infection against usual hospital care in the UK. As of June 25, 2020, 11 841 patients have been enrolled in the RECOVERY trial across 176 hospitals. Rapid recruitment for the trial was made possible due to unprecedented leadership and national-level collaborations across the UK. The RECOVERY trial,

***Panel 3:* REMAP-CAP trial**

The Randomised, Embedded, Multifactorial, Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP; NCT02735707) is a platform trial evaluating the effects of a range of interventions to improve the outcomes of patients admitted to the intensive care unit (ICU) with community-acquired pneumonia.[83] The adaptive trial design was planned, before the COVID-19 pandemic, for the evaluation of multiple